DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-23,32-33) in the reply filed on 2/13/08 is acknowledged. It is noted that applicant elected the peptide INSL3 (SEQ ID NO:7) as the peptide. Applicant also stated that they elected the A-chain of relaxin 1 and the reporter being a fluorescent reporter.

Since the election of species as stated in the written reply of 2/13/08 was unclear applicants representative Joseph Snyder was contacted on 3/10/08 as noted in the attached interview summary. Briefly, it was noted that the peptide INSL3 (SEQ ID NO:7) as identified in the written reply of 2/13/08 is a linear peptide, not a cyclic peptide as recited in claim 1. Further, it was noted that it was unclear which specific conjugate was elected and it was unclear which claims read on the elected invention. It was agreed that the peptide INSL3 (SEQ ID NO:7) would be searched as the elected peptide of the instant invention and that the peptide would be searched with respect to the claim limitations recited in claims 1 and 3. It was agreed that the species examined would be the peptide INSL3 (SEQ ID NO:7) as recited in claims 1 and 3 (i.e. no conjugate).

The traversal (as recited in the written reply of 2/13/08) is on the ground(s) that claims can be examined together without undue burden. Applicants argue that no undue burden exists in the present case.

This is not found persuasive because there would be a search and examination burden because the inventions require a different field of search (for example, searching different

electronic resources or employing different search queries); the prior art applicable to one invention would not likely be applicable to another species, and the inventions are likely to raise different non-prior art issues under 35 USC 101 and/or 35 USC 112, first paragraph.

The requirement is still deemed proper and is therefore made FINAL.

In the instant case the elected species was found in the prior art. As such the examination is limited to the generic claim and claims to the elected species. In the instant case, claims 1,3,32-33 read on the elected species.

Claims 2,4-31,34-49 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention/species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/13/08.

Claims 1,3,32-33 are under consideration.

Claim Objections

Claims 32-33 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). In the instant case claim 3 is a multiple dependent claim. Claim 32 and 33 both depend from claim 3.

Accordingly, claims 32-33 have not been further treated on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and dependent claim 3 are drawn to monomeric cyclic peptide analogues. Claim 3 states that the analogues are modified from a sequence set forth in SEQ ID NO:7. The metes and bounds of the claims remain unclear. In particular, no specific definition has been set forth to identify analogues nor is there an art-recognized definition of analogue. Further, no specific degree or type of modification has been set forth for all the possible analogues. Taken together one would not recognize what falls within the scope of the instant invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus …") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a

substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to cyclic peptide analogues. Claim 3 states that the analogue is modified from a sequence set forth in SEQ ID NO:7

(1) Level of skill and knowledge in the art:

The level of skill in the art is high.

(2) Partial structure:

Sections 0024,0069 of the specification (PGPub 20070004619) state that one or more amino acids within the peptide analogue sequence are optionally substituted. Section 0072 of the

specification states that individual amino acids can be replaced by analogous structures, for example alkylmalonyl groups. Sections 0063-0068 of the specification state that a wide range of chemical linking groups can be used and a range of cyclization processes can be used.

In considering the possible variability, if SEQ ID NO:7 (31 amino acids) was substituted at every position except for the cysteine residues with any of the 20 natural amino acids (i.e. an analog) there would be 20^{29} possible analogues. If there are substitutions with alkylmalonyl groups as discussed in section 0072 or if fusion compounds are considered the variability further increases. Hence, there is substantial variability in the genus.

Figure 3 shows 3 cyclic peptides (SEQ ID NOs: 11-13). However, the 3 examples provided are not representative of the genus (which includes well over 20^{29} possible analogues).

Since there are a substantial variety of peptides possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

(3) Physical and/or chemical properties and (4) Functional characteristics:

Claim 1 describes the analogues as being of a B-chain of a relaxin superfamily member protein which binds to a biological target. Section 0012 of the specification (PGPub 20070004619) states that ideally the analogues would include ligands, such as agonists, reverse agonists, partial agonists, mixed agonists/antagonists and full antagonists, which bind at the relaxin superfamily member receptors and initiate, inhibit, activate, or otherwise control, the biological activities of members of this protein superfamily. However, there is no disclosed correlation between structure and function for all of the analogues. Further, what constitutes an

analogue is not clearly set forth. In particular, no common sequence or common core is taught for the analogs. It is noted that claim 3 recites a particular sequence but the claim is drawn to an analogue modified from that sequence. As such, there is no common core sequence.

(5) Method of making the claimed invention:

The specification (specifically example 1) describes the solid-phase synthesis of peptides, however the specification fail to describe the synthesis of a representative number of analogues.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1,3 is/are broad and generic, with respect to all possible analogues encompassed by the claims. The possible structural variations are many. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the peptides beyond those peptides specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of peptides identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of peptides embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed

that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1,3 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Schwabe et al. (US 5,911,997) teach (Figure 1 and Figure 1 caption column 3 lines 43-49) a peptide identified as the relaxin-like factor. The peptide includes the B-chain portion identified as SEQ ID NO:4 (i.e. PTPEMREKLCGHHFVRALVRVCGGPRWSTEA) which includes the primary sequence (without the disulfide bonds) identified as SEQ ID NO:7 of the instant invention. The peptide of Schwabe is a cyclic monomeric peptide (Figure 1). The peptide of Schwabe is an analog of SEQ ID NO:7 (a linear peptide) of the instant invention since the peptide of Schwabe includes disulfide bonds and cyclization.

Schwabe teach that the relaxin-like factor (for example as shown in Figure 1) is from a human source (human Ley I-L) (column 3 lines 7-12 and column 2 lines 26-50).

There is no indication that the peptides of the current invention have been isolated or removed from a naturally occurring environment. The claimed subject matter therefore reads on a product of nature.

Although unclear (see 112 2nd above) the claims have been interpreted broadly (see MPEP 2111) such that analogues include any amount of modifications.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,3 are rejected under 35 U.S.C. 102(b) as being anticipated by Schwabe et al. (US 5,911,997).

Schwabe et al. (US 5,911,997) teach (Figure 1 and Figure 1 caption column 3 lines 43-49; claim 1) a peptide identified as the relaxin-like factor. The peptide includes the B-chain portion identified as SEQ ID NO:4 (i.e. PTPEMREKLCGHHFVRALVRVCGGPRWSTEA) which includes the primary sequence (without the disulfide bonds) identified as SEQ ID NO:7 of the instant invention. The peptide of Schwabe is a cyclic monomeric peptide (Figure 1). The peptide of Schwabe is an analog of SEQ ID NO:7 (a linear peptide) of the instant invention since the peptide of Schwabe includes disulfide bonds and cyclization thus meeting the limitations of claims 1,3 of the instant invention.

It is noted that claim 1 states that the peptide modulates an activity of the biological target. Section 2112.01 of the MPEP states that products of identical chemical compositions can

not have mutually exclusive properties. In the instant case, the peptide of Schwabe meet the claim limitations so the peptide necessarily has the claimed activity.

Although unclear (see 112 2nd above) the claims have been interpreted broadly (see MPEP 2111) such that analogues include any amount of modifications.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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